



## Original article

## Can aortic atherosclerosis or epicardial adipose tissue volume be used as a marker for predicting coronary artery disease?



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## ABSTRACT

**Purpose:** To investigate whether aortic atherosclerosis or epicardial adipose tissue (EAT) volume on multidetector computed tomography (CT) can predict the presence of significant coronary artery disease (CAD).

**Materials and methods:** Coronary CT angiography was performed in 202 cases of CAD that were known or based on suspicion. Based on coronary CT angiography results, the patients with significant stenosis ( $\geq 50\%$ ) and without significant stenosis ( $< 50\%$ ) were compared in terms of demographic characteristics, traditional cardiovascular risk factors, aortic atherosclerosis, and EAT volume.

**Results:** Significant coronary artery stenosis was detected in 92 cases (45.5%). Although EAT volume was higher in the patients with significant stenosis, the difference between the two groups was not statistically significant. The presence of calcification in the descending aorta was significantly higher in the patients with significant stenosis than the patients without significant stenosis (50.4% and 15.4%, respectively,  $p = 0.0001$ ). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy rates of the presence of calcification in the descending aorta in predicting the presence of significant coronary artery stenosis were respectively found as 53.8%, 84.4%, 74.6%, 68.1%, and 70.3%. The sensitivity, specificity, PPV, NPV, and accuracy rates of the  $\geq 2.45$  mm wall thickness of the descending aorta in predicting the presence of significant coronary artery stenosis were respectively found as 75.3%, 74.3%, 71.4%, 77.9%, and 74.8%.

**Conclusion:** There is a strong relationship between thoracic aortic atherosclerosis and CAD. However, the relationship between EAT volume and CAD is not significant. The presence of aortic atherosclerosis can be used as an additional marker together with traditional cardiovascular risk factors for predicting CAD.

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## Introduction

Aortic atherosclerosis, which plays a key role in the pathophysiology of ischemic stroke, can be used as a marker for coronary artery disease (CAD) [1–6]. Studies conducted with transesophageal echocardiography showed that thoracic aortic atherosclerosis was associated with cardiovascular risk factors and CAD [2]. In the studies conducted with magnetic resonance (MR) imaging, a relationship was detected between the prevalence of thoracic and abdominal aortic plaques and the severity of CAD [7]. Furthermore, in a study performed using electron-beam computed tomography (CT), Takasu et al. [8] reported that the thoracic aortic calcification detected in CT was highly specific for obstructive CAD.

Epicardial adipose tissue (EAT) is a type of visceral adipose tissue that functions like an endocrine organ by secreting adipocytokine and certain other hormones that contribute to the atherosclerotic process. It is considered that the epicardial adipose tissue contributes to the pathogenesis of CAD due to its closeness to the adventitia of the coronary arteries. The relationship between increased EAT and CAD was found to be significant in some studies. Sarin et al. [9] reported that increased ( $> 100$  mL) EAT volume could be used as a non-invasive marker for CAD, just as calcium score. However, since there are also studies [10–12] reporting that there is no significant relationship between increased EAT and CAD, studies that involve larger patient populations are required in order to obtain more precise data on this topic.

Since coronary CT angiography is reliable and non-invasive in the detection of CAD, it is a procedure with a gradually increasing clinical use despite radiation exposure. Coronary CT angiography provides information not only regarding coronary atherosclerosis, but also about thoracic aortic atherosclerosis within the scan area.

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Recently, it was found in the studies conducted with multidetector CT that descending aortic atherosclerosis was observed at a higher rate in cases with coronary artery stenosis compared to those without coronary artery stenosis [3,8,13–17]. Since thoracic or abdominal aortic atherosclerosis can be easily detected through routine thorax and abdomen CT examinations, it is important to determine whether aortic atherosclerosis can be used as a detection marker for CAD.

In the present study, which we conducted on a large patient population, we aimed to investigate the relationship among CAD and aortic atherosclerosis, EAT volume, and traditional cardiovascular risk factors and to determine whether aortic atherosclerosis or EAT volume can be used as a marker for predicting the presence of CAD.

## Materials and methods

### *Patient population*

A total of 419 cases of CAD that were known or based on suspicion underwent a coronary CT angiography examination from December 2011 to November 2012 at our institution. Overall, 201 patients who did not undergo a coronary artery calcium (CAC) score examination before coronary CT angiography and who had a coronary stent or bypass grafts were excluded from the study. Sixteen patients were excluded from the study when the coronary CT angiography examination was suboptimal, and the coronary arteries could not be sufficiently evaluated. A total of 202 cases [73 females, 129 males; median age  $55.4 \pm 12.4$  years (range, 26–84 years)] were included in the study. Informed consent was obtained from all the patients, and the study was approved by the local ethics committee of our hospital.

### *Multi detector CT data acquisition*

A 64-detector CT scanner (Aquilion, Toshiba Medical Systems, Tokyo, Japan) and the same protocol were used for the examination of the patients. In the CAC score examination, an area from the carina level to the heart base was scanned with prospective electrocardiogram (ECG) triggering at a slice thickness of 3 mm (tube voltage, 120 kV; tube current, 300 mA). In the coronary CT angiography examination, an 80–100 mL iodinated contrast agent (Iomeron, Iomeprol 400 mgI/mL, Bracco, Milan, Italy or Iopromid, Ultravist 370 mgI/mL, Schering AG, Berlin, Germany) was administered through an 18–20 G cannula, which was placed in a cubital vein. Then, 40 mL saline was administered at the same rate. The optimal scan time was determined using the automatic bolus tracking method (Sure Start, Toshiba Medical Systems). The region of interest was placed over the descending aorta, and an adjustment was made to ensure that the scanning would automatically start when the maximum contrast reached 180 HU. The coronary CT angiography examination parameters were as follows: collimation, 64 mm  $\times$  0.5 mm; tube voltage, 120 kV; tube current, 400–500 mA; tube rotation time, 400 ms; slice thickness, 0.5 mm; and increment, 0.3 mm. A retrospective ECG-gated technique was used for the reconstruction of the images. The raw data that were obtained from the coronary CT angiography examination were reconstructed at the 75% phase (mid-diastolic phase) of the R–R interval using a slice thickness of 0.5 mm and an increment of 0.3 mm. For the cases in which this phase was not optimal for the image analysis, additional reconstructions were obtained at the 35–85% phase of the R–R interval.

### *Multi detector CT image analysis*

Two- and three-dimensional images were rendered using multiplanar reformatting, curved planar reformatting, maximum

intensity projection, and volume rendering methods by transferring the obtained axial CT angiography images to a separate workstation (Vitrea 2, Vital Images, Minnetonka, MN, USA).

The Agatston method was used in the quantification of the CAC score. The left main coronary artery (LMCA), the left anterior descending (LAD) artery, the left circumflex (LCX) artery, and the right coronary artery (RCA) were examined for the presence of atherosclerotic plaques in the non-contrasted axial slices throughout their entire trace. The foci of the CAC were detected by one of two experienced radiologists and scored using semi-automatic commercial software to detect at least three contiguous pixels (voxel size, 1.03 mm<sup>3</sup>) with a peak density  $\geq 130$  HU within a coronary artery.

The patients were divided into two groups according to the presence or absence of calcification in any region of the descending aortic wall.

For the evaluation of aortic wall thickness the cardiac CT angiography examinations were used. Wall measurements were performed using a defined window level setting (center 250, width 1000 HU) to optimize the wall visualization. Before the measurements, the images were magnified to about 400%. The maximum wall thickness of the descending aorta was measured perpendicular to the center of the vessel.

EAT was defined as the adipose tissue between the surface of myocardium and visceral layer of the pericardium (epicardium). Quantification of total EAT volume was done on a separate workstation (Advanced Workstation 4.2, GE, Milwaukee, WI, USA) with dedicated software (Volume Viewer, GE). A semi-automated volumetric method was developed for quantification of EAT. Using the 3-mm thick axial slices used for calcium scoring, we manually traced the outer border of the epicardium in every fourth slice starting from the aortic root to the apex of the heart. The number of slices that had to be traced manually ranged from 6 to 12 in each patient. The computer software then automatically interpolated and traced the epicardium in all the slices interposed between the manually traced slices. Total number of slices traced manually or automatically ranged from 30 to 40 in each patient, depending on the heart size. All the automatically traced slices were examined and verified for accuracy. Two histograms were generated to depict total cardiac volume and EAT volume. Fat voxels were identified using threshold attenuation values of –30 to –250 HU.

A modified American Heart Association classification that divided the coronary arterial system into 16 segments was used in the evaluation of the coronary arteries. In the coronary CT angiography images, each coronary artery segment was evaluated for the presence of a wall irregularity and/or the presence of an atherosclerotic plaque.

Each identified coronary artery lesion was assessed for stenosis severity along multiple longitudinal, transverse, and oblique axes with the use of multiplanar reconstructions, thin-slab maximum intensity projections, and curved reconstruction techniques. Coronary artery plaque was defined as any clearly discernible structure attributable to the coronary artery wall in at least two independent image planes. The degree of stenosis that was caused by the plaques was found by comparing the lumen diameter of the narrowest segment with that of a more proximal or distal normal segment. Stenoses were classified as non-significant in cases with a mean lumen diameter reduction of  $<50\%$  or significant in cases with a mean lumen diameter reduction of  $\geq 50\%$  in two orthogonal projections. The patient groups with or without plaque as observed in coronary CT angiography were classified according to the demographic characteristics, the cardiovascular risk factors, the presence of aortic calcification in the descending aorta, the wall thickness of the descending aorta, and EAT volume and were statistically compared.

## Statistical analysis

Statistical analyses were performed using commercially available software (Statistical Package for Social Sciences, version 15.0, SPSS Inc., Chicago, IL, USA). The continuous variables were expressed as the means  $\pm$  standard deviation (SD). The differences in the mean values between the two groups were compared using the unpaired *t* test. Comparisons of the categorical variables between the two groups were performed using the chi-square test. Multiple logistic regression analyses were used to assess the associations with the presence of coronary plaque. These analyses were performed for the entire study population and the gender-specific population. Receiver operating curves (ROC) were used to establish cut-off levels of maximum wall thickness of descending aorta for CAD risk assessment. The 95% confidence interval was calculated for each odds ratio. Values of  $p < 0.05$  were considered significant. On multivariate logistic regression analysis with backward elimination  $p < 0.10$  was considered significant.

## Results

On the coronary CT angiography, significant stenosis was not seen in 110 (54.5%) of the 202 cases, whereas significant stenosis was observed in 92 (45.5%) of the cases. Of the cases without significant stenosis, 56 (50.9%) were males and 54 (49.1%) were females, while 73 (79.3%) of the cases with significant stenosis were males and 19 (20.7%) were females. Univariate logistic regression analysis showed that the detection rate of significant

coronary artery stenosis in males was 3.45 times higher compared to females ( $p = 0.0001$ ). The mean age of the cases with significant stenosis ( $60.8 \pm 10.6$  years) was significantly higher compared to those without significant stenosis ( $50.7 \pm 12.4$  years) ( $p = 0.0001$ ). The prevalence of diabetes mellitus, hypertension, family history, smoking, and dyslipidemia was significantly higher in cases with significant stenosis ( $p = 0.003$ ,  $0.011$ ,  $0.044$ ,  $0.001$ , and  $0.006$ , respectively). The demographic characteristics of the patients with and without plaques detected in coronary CT angiography and the prevalence of the cardiovascular risk factors are presented in Table 1.

Although EAT volume was found to be higher in the group with significant coronary artery stenosis, the difference between the two groups was not statistically significant ( $92.6 \pm 40.4 \text{ cm}^3$ ,  $84.3 \pm 35.5 \text{ cm}^3$ , respectively,  $p = 0.123$ ) (Table 1).

The presence of calcification in the descending aorta was detected in 54.3% ( $n = 50$ ) of the cases with significant stenosis and in 15.4% ( $n = 17$ ) of the cases without significant stenosis and the difference between the cases was found to be statistically significant ( $p = 0.0001$ ). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy rates of the presence of calcification in the descending aorta in predicting the presence of significant coronary artery stenosis were respectively found as 53.8%, 84.4%, 74.6%, 68.1%, and 70.3% (Table 2).

The wall thickness of the descending aorta was significantly higher in the group with significant coronary artery stenosis compared to that without significant stenosis ( $3.3 \pm 1.1 \text{ mm}$ ,  $2.2 \pm 1.9 \text{ mm}$ , respectively,  $p = 0.0001$ ) (Fig. 1). The results of the

**Table 1**

Baseline characteristics and prevalence of cardiovascular risk factors of study patients with (+) or without (–) significant stenosis in coronary computed tomography angiography.

	Entire cohort ( $n = 202$ )			<i>p</i>
	All	Stenosis (–)	Stenosis (+)	
<i>N</i> (%)	202 (100)	110 (54.5)	92 (45.5)	–
Male	129 (63.9)	56 (50.9)	73 (79.3)	0.0001
Age (years)	$55.3 \pm 12.4$ (26–84)	$50.7 \pm 12.4$	$60.8 \pm 10.6$	0.0001
Diabetes mellitus	50 (24.7)	18 (16.4)	32 (34.8)	0.003
Hypertension	85 (42.1)	37 (33.6)	48 (52.2)	0.011
Familial history	34 (16.8)	13 (11.8)	21 (22.8)	0.044
Smoking	67 (33.2)	24 (21.8)	43 (46.7)	0.001
High LDL	63 (31.2)	28 (25.4)	35 (38)	0.068
High total cholesterol	73 (36.1)	30 (27.3)	43 (46.7)	0.006
Low HDL	75 (37.1)	34 (30.9)	41 (44.6)	0.059
High triglyceride	38 (18.9)	20 (18.2)	18 (19.6)	0.826
CAC score >0	113 (55.9)	25 (22.7)	88 (95.6)	0.0001
Aortic calcification	67 (33.2)	17 (15.4)	50 (54.3)	0.0001
AWT (mm)	$2.7 \pm 1.6$ (1.1–6.0)	$2.2 \pm 1.9$	$3.3 \pm 1.1$	0.0001
EAT volume ( $\text{cm}^3$ )	$88.1 \pm 38$ (17.5–231)	$84.3 \pm 35.5$	$92.6 \pm 40.4$	0.123

LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; CAC, coronary artery calcium; AWT, aortic wall thickness; EAT, epicardial adipose tissue; SD: standard deviation. Data are given as *n* (%) or mean  $\pm$  SD.

**Table 2**

The accuracy rates of coronary artery calcium (CAC) score, aortic calcification, and aortic wall thickness (AWT) in the prediction of the presence of significant coronary artery stenosis of study patients with (+) or without (–) significant stenosis in coronary computed tomography angiography.

Clinical parameters	Stenosis (–) <i>N</i> (%)	Stenosis (+) <i>N</i> (%)	<i>p</i>	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
CAC score								
0	84 (77.1)	5 (5.4)	0.0001	94.6	77.1	77.9	94.4	85.1
>0	25 (22.9)	88 (94.6)						
Aortic calcification								
(–)	92 (84.4)	43 (46.2)	0.0001	53.8	84.4	74.6	68.1	70.3
(+)	17 (15.6)	50 (53.8)						
AWT (mm)								
<2.45	81 (74.3)	23 (24.7)	0.0001	75.3	74.3	71.4	77.9	74.8
$\geq 2.45$	28 (25.7)	70 (75.3)						

PPV, positive predictive value; NPV, negative predictive value.



**Fig. 1.** A 62-year-old man presented with angina pectoris and two risk factors, which are hypertension and smoking. Curved planer reformatted computed tomography angiography image (a) shows a calcified soft plaque (short arrows) causing a significant stenosis and calcified plaques (long arrow) causing nonsignificant stenosis in the left anterior descending artery (LADA). Axial image (b) reveals that the maximum wall thickness of the descending aorta (DAo) is 3.7 mm. Ao, aorta.

ROC analysis revealed that the cut-off value for the wall thickness of the descending aorta was 2.45 mm and the area under the curve was 0.825 (Fig. 2). The sensitivity, specificity, PPV, NPV, and accuracy rates of the  $\geq 2.45$  mm wall thickness of the descending aorta in predicting the presence of significant coronary artery stenosis were respectively found as 75.3%, 74.3%, 71.4%, 77.9%, and 74.8% (Table 2).

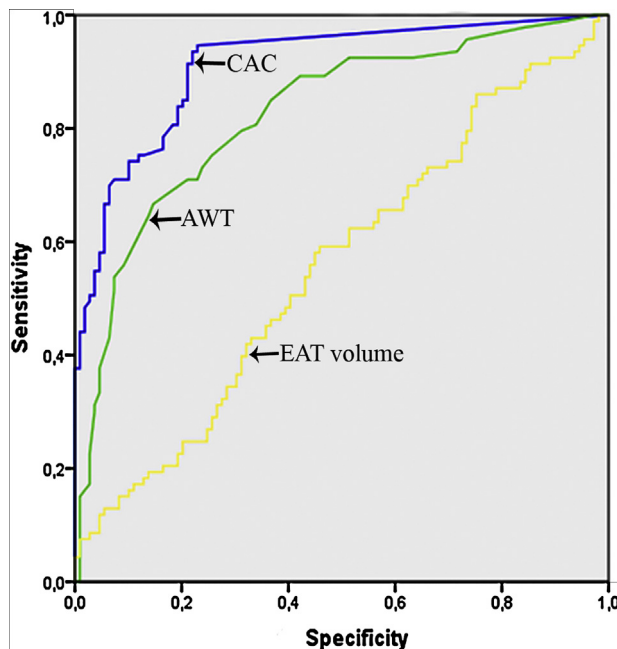
When patients with a positive CAC score were grouped as  $\leq 10$ , 11–100, 101–400, and  $\geq 401$ , the rates of calcification in the descending aorta for these groups were respectively found as 15.3%, 25.7%, 46.4%, and 73.2% and it was observed that the rate of calcification in the descending aorta increased as CAC score

increased ( $p = 0.0001$ ). Similarly, the ratio of a wall thickness of the descending aorta of  $\geq 2.45$  mm also increased as CAC score increased (35.7%, 45.7%, 60.7%, and 73.2%, respectively,  $p = 0.0001$ ). The relationship between the increase in calcium score and EAT volume was not found to be statistically significant ( $83.5 \pm 35.7$ ,  $88.6 \pm 35.1$ ,  $87.8 \pm 38.3$ ,  $99 \pm 30$ , respectively,  $p = 0.186$ ) (Table 3).

Calcification was present in the descending aorta in 15.6% of the cases without significant stenosis, 47.2% of the cases with one-vessel stenosis, 52.2% of the cases with two-vessel stenosis, and 81.2% of the cases with three-vessel stenosis. Statistical evaluation showed that the rate of calcification in the descending aorta significantly increased as the number of vessels with significant stenosis increased ( $p = 0.0001$ ). The wall thickness of the descending aorta was  $\geq 2.45$  mm in 25.7% of the cases without significant stenosis, in 77.4% of the cases with one-vessel stenosis, in 65.2% of the cases with two-vessel stenosis, and in 81.2% of the cases with three-vessel stenosis. Statistical evaluation showed that the ratio of a wall thickness of the descending aorta of  $\geq 2.45$  mm significantly increased as the number of vessels with significant stenosis increased ( $p = 0.0001$ ).

According to the results of the multivariate logistic regression analysis, age of  $\geq 70$  years was found to be a significant risk factor for both descending aorta calcification ( $p = 0.001$ ) and for a wall thickness of the descending aorta of  $\geq 2.45$  mm ( $p = 0.031$ ), while hypertension was detected as a significant risk factor for descending aorta calcification ( $p = 0.033$ ) and a borderline significant risk factor for a wall thickness of the descending aorta of  $\geq 2.45$  mm ( $p = 0.053$ ).

According to the results of the univariate logistic regression analysis, age of  $\geq 70$  years, male gender, diabetes, hypertension, smoking, family history, CAC score, descending aorta calcification, and a wall thickness of the descending aorta of  $\geq 2.45$  mm were found to be significant risk factors for significant coronary artery stenosis (for all,  $p < 0.001$ ). According to the results of the multivariate logistic regression analysis with backward elimination, diabetes ( $p = 0.024$ ), hypertension ( $p = 0.081$ ), smoking ( $p = 0.044$ ), family history ( $p = 0.015$ ), CAC score ( $p = 0.001$ ), and a wall thickness of the descending aorta of  $\geq 2.45$  mm ( $p = 0.001$ ) were found to be significant risk factors for significant CAD (Table 4).



**Fig. 2.** Receiver operating curve analysis delineating the discriminative power of maximum wall thickness of the descending aorta (AWT), coronary artery calcium (CAC) score, and epicardial adipose tissue (EAT) volume to identify the presence of significant coronary artery stenosis. The area under the receiver operating curve was  $0.825 \pm 0.03$  (CI: 0.767–0.883) for AWT  $\geq 2.45$  mm,  $0.912 \pm 0.02$  (CIU: 0.872–0.952) for CAC score, and  $0.557 \pm 0.04$  (CI: 0.477–0.636) for EAT volume.



**Table 3**

Correlation between aortic calcification, aortic wall thickness (AWT), epicardial adipose tissue (EAT) volume, and coronary artery calcium (CAC) score.

Clinical parameters	CAC score				p
	≤10	11–100	101–400	≥401	
Aortic calcification					
(–)	83 (84.7)	26 (74.3)	15 (53.6)	11 (26.8)	0.0001
(+)	15 (15.3)	9 (25.7)	13 (46.4)	30 (73.2)	
AWT (mm)					
<2.45	63 (64.3)	19 (54.3)	11 (39.3)	11 (26.8)	0.0001
≥2.45	35 (35.7)	16 (45.7)	17 (60.7)	30 (73.2)	
EAT volume (cm <sup>3</sup> )	83.52 ± 35.7	88.6 ± 35.1	87.8 ± 38.3	99 ± 30	0.186

Data are given as n (%) or mean ± SD.

**Table 4**Predictors of the presence of significant coronary artery stenosis on multivariate logistic regression analyses with backward elimination ( $p < 0.10$  is considered significant).

Clinical parameters	Odds ratio (95% CI)	p
Diabetes mellitus	3.874 (1.196–12.550)	0.024
Hypertension	2.604 (0.890–7.615)	0.081
Smoking	2.939 (1.030–8.389)	0.044
Familial history	4.089 (1.32–12.666)	0.015
CAC score >0	60.280 (13.940–260.676)	0.001
AWT ≥ 2.45 mm	11.860 (3.749–37.512)	0.001

CAC, coronary artery calcium; AWT, aortic wall thickness; CI, confidence interval.

## Discussion

The relationship between CAD and the frequency and distribution of thoracic aortic atherosclerotic plaques was clearly presented in previous studies. In a postmortem study conducted by Tobler et al. [18], the presence of atherosclerotic plaques larger than 8 mm was detected in the ascending aorta in 38% of patients with known CAD. In another study conducted on 111 female cases using transesophageal echocardiography, Tribouilloy et al. [19] found the sensitivity, specificity, PPV, and NPV rates of the presence of thoracic aortic plaques in predicting significant CAD respectively as 83%, 86%, 62%, and 95% and stated that thoracic aortic plaques were a strong marker particularly for the absence of significant CAD. In an MR imaging study [7], the detection rate of atherosclerotic plaques in the thoracic aorta in cases with and without CAD was respectively found as 71% and 29% and the detection rate of atherosclerotic plaques in the abdominal aorta was respectively found as 95% and 75%. As the result of the aforementioned study, the researchers concluded that thoracic aortic plaques were an independent factor for CAD. Similarly, in a study conducted using CT, Takasu et al. [20] found that thoracic atherosclerotic plaques were more closely related to CAD compared to abdominal aorta plaques.

In a study conducted using electron beam CT to investigate the relationship between wall calcification, which is an indicator of aortic atherosclerosis, and CAD, it was reported that aortic calcification was a risk factor independent of CAC score for CAD [21]. There are studies stating that when additional aortic findings are taken into consideration in patients who underwent thorax CT due to non-cardiac reasons, certain related parameters could be a risk indicator for cardiovascular disease. In a study conducted considering that the ancillary aortic findings detected on routine thorax CT images could be a predictor for cardiovascular disease and preventive measures could be applied, Gondrie et al. [22] evaluated the aorta in terms of wall calcification, wall irregularity, plaque and tortuosity. The researchers determined aortic wall

calcification as the most valuable finding for cardiovascular risk evaluation due to its detectability in non-contrast CT. Wong et al. [23] conducted a study on 2303 asymptomatic adults to compare the ability of CAC score and thoracic aortic calcification in predicting CAD and reported that there was a relationship between thoracic aortic calcification and CAD but this relationship was not as strong as that between CAC and CAD. The researchers detected thoracic aortic calcification in 63% of the patients with coronary artery stenosis and in 22% of the patients without coronary artery stenosis and found the sensitivity and specificity of thoracic aortic calcification in predicting significant coronary artery stenosis as 56% and 72%, respectively. In this study, a relationship was detected between thoracic aortic calcification and age, hypertension, smoking and dyslipidemia. In our study, we detected thoracic aortic calcification in 54.3% of the cases with significant coronary artery stenosis and in 15.4% of the cases without significant coronary artery stenosis. We found the sensitivity, specificity, PPV, NPV, and accuracy rates of the presence of thoracic aortic calcification in predicting the presence of significant coronary artery stenosis as 53.8%, 84.4%, 74.6%, 68.1%, and 70.3%, respectively. As the result of the multivariate logistic regression analysis, we found age (≥70 years) and hypertension as significant risk factors for thoracic aortic calcification. When we grouped the patients with a positive CAC score as ≤10, 11–100, 101–400, and ≥401, we found the rates of calcification in the descending aorta for these groups respectively as 15.3%, 25.7%, 46.4%, and 73.2% and we detected that the rate of calcification in the descending aorta significantly increased as CAC score increased. We found that calcification was present in the descending aorta in only 15.6% of the cases without significant stenosis, in 47.2% of the cases with one-vessel stenosis, in 52.2% of the cases with two-vessel stenosis, and in 81.2% of the cases with three-vessel stenosis and we detected that the rate of calcification in the descending aorta significantly increased as the number of vessels with significant stenosis increased.

It was shown in previous studies that the increase in artery wall thickness could have a predictive value for cardiovascular diseases. In prospective studies conducted on this topic, it was detected that increased carotid intima-media thickness was an independent marker for CAD and ischemic stroke. In a transesophageal echocardiography study, Bae et al. [24] found that there was a correlation between descending aorta wall thickness and the number of coronary arteries with stenosis. Couturier et al. [25] conducted a study by measuring the intima-media thickness of the aortic arch through the supraclavicular window with B-mode ultrasound and showed that increased aortic arch intima-media thickness was a strong predictor for CAD. In a study conducted by Jeltsch et al. [13] on 160 patients using multidetector CT, the sensitivity, specificity, and PPV rates of the wall thickness of the descending aorta in predicting CAD were respectively found as 55%, 81%, and 83.5% for a wall thickness of 2.4 mm, as 42.2%, 91.4%,

and 89.6% for a wall thickness of 2.6 mm, and as 27.5%, 96.6%, and 93.3% for a wall thickness of 3 mm. The researchers pointed out that the PPV of a wall thickness of the descending aorta of  $\geq 2.6$  mm in predicting CAD was 100% in cases with two or more cardiovascular risk factors. Besides, they stated that calcification was detected in the descending aorta in 91% of the patients who had coronary artery plaques regardless of the degree of stenosis and concluded that there was a close relationship between aortic atherosclerosis and coronary atherosclerosis. In our study, we found that wall thickness of the descending aorta was significantly higher in cases with significant coronary artery stenosis compared to those without stenosis. In our study, we found the sensitivity, specificity, PPV, NPV, and accuracy rates of a wall thickness of the descending aorta of  $\geq 2.45$  mm in predicting the presence of significant coronary artery stenosis as 75.3%, 74.3%, 71.4%, 77.9%, and 74.8%, respectively. As the result of the multivariate logistic regression analysis, we detected age ( $\geq 70$  years) and hypertension as significant risk factors for increased descending aorta wall thickness. We found that as CAC score increased or the number of vessels with significant stenosis increased, the ratio of an increased wall thickness ( $\geq 2.45$  mm) also increased. In line with previous studies, the results of our study also showed that there was a highly strong relationship between aortic atherosclerosis and CAD.

In a multidetector CT study, Yorgun et al. [3] scored the aortic plaques at the proximal, mid, and distal segments of the descending aorta and divided them into 4 groups by the percentage of the luminal surface ( $<25\%$ ,  $25\text{--}50\%$ ,  $50\text{--}75\%$ ,  $>75\%$ ) and found that the total plaque score was higher in cases with significant coronary artery stenosis. Furthermore, they found that the total plaque score of the descending aorta significantly increased as the number of atherosclerotic coronary artery segments increased and stated that aortic atherosclerosis was an independent risk factor for coronary artery stenosis. The results of their univariate logistic regression analysis revealed that there was a significant relationship between the atherosclerosis present in any segment of the thoracic aorta and CAD, whereas the results of their multivariate logistic regression analysis showed that the relationship between high total plaque score, that is, the aortic plaques existing in a number of segments of the thoracic aorta, and CAD was a risk factor independent of the other cardiovascular risk factors. In our study, we measured the wall thickness at the thickest section of the descending aorta within the examination area and found that a thickness of  $\geq 2.45$  mm could be used as a marker in predicting CAD together with other cardiovascular risk factors.

In a study conducted with electron-beam CT, Takasu et al. [8] found that the presence of aortic atherosclerotic plaques was a predictor independent of coronary artery calcification for obstructive CAD. The researchers found the sensitivity and specificity of the presence of aortic plaques in predicting coronary artery stenosis as 89% and 63%, respectively, whereas these rates were 56% and 72% for aortic calcification and they stated that aortic calcification was highly specific for obstructive CAD. The researchers pointed out that the increase in the wall thickness of the thoracic aorta together with calcification had a higher predictive value for CAD. In our study, we observed that either CAC score  $>0$  or descending aortic calcification was positive in 98.9%, while CAC score  $>0$  and descending aortic calcification were both positive in 49.5% of the cases with significant coronary stenosis. Similarly, either CAC score  $>0$  or a wall thickness of the descending aorta of  $\geq 2.45$  mm was positive in 100% of the cases with significant coronary stenosis, whereas both were positive in 69.9% of the cases. Similar to the results obtained by Takasu et al. [8], we also determined that the increase in the wall thickness of the thoracic aorta together with calcification had a higher predictive value for CAD.

EAT is not only a fat depot but also an endocrine tissue that secretes adipocytokines and certain other hormones (tumor necrosis factor, interleukin-6, 8, 10) that contribute to the atherosclerotic process. Discordant results were obtained in the studies conducted to evaluate the relationship between EAT thickness and CAD [9–12]. While the relationship between EAT thickness and CAD was found to be significant in some studies, other researchers reported that there was no significant relationship between coronary disease and EAT [10]. Studies showed that the clinical significance of measuring EAT thickness alone is limited and the volumetric measurement of EAT is required [9,26–28]. Multidetector CT is a modality that provides more precise results in measuring EAT volume compared to echocardiography and MR imaging. In a multidetector CT study, Djaberi et al. [9,26] found that EAT volume was significantly higher in cases with a CAC score  $>10$  and/or with coronary atherosclerosis compared to cases with a CAC score  $\leq 10$  and/or without coronary atherosclerosis and reported that EAT volume could be used as an independent marker for predicting coronary atherosclerosis. In another multidetector CT study, it was found that increased EAT volume was related to obstructive CAD and soft tissue plaques [27]. In a study on the relationship between EAT thickness and thoracic aortic atherosclerosis, Yorgun et al. [28] found that there was a strong relationship between descending aorta atherosclerosis and EAT thickness in cases with critical coronary artery stenosis. In our study, we found that there was not a significant difference between cases with and without significant stenosis in terms of mean EAT volume ( $92.6\text{ cm}^3$ ,  $84.3\text{ cm}^3$ , respectively,  $p = 0.123$ ). When we evaluated the relationship between CAC score and EAT volume, we found that EAT volume increased as CAC score increased, but this increase was not statistically significant. The results of our study showed that EAT volume could not be used as a marker for predicting significant coronary disease.

Our study has certain limitations. First, since our population consisted of patients suspected of having CAD, cardiovascular risk rates were found to be higher compared to those of a randomly selected population. Second, in the present study, we did not find the opportunity to compare the coronary CT angiography results with catheter coronary angiography results. When compared by taking lumen-based catheter coronary angiography as reference, multidetector CT coronary angiography has a highly distinctive capacity in detecting obstructive CAD. However, despite new improved scanning devices, the spatial and temporal resolution of multidetector CT is limited. This limits the detection and quantification of non-calcified plaques in coronary arteries and distal segments may not be evaluated with adequate accuracy in many cases even with 64-detector CTs. Third, in our study, aortic atherosclerosis was evaluated only through the descending aorta, which fell within the imaging area. For this reason, the atherosclerotic process in the whole thoracic aorta could not be evaluated. Due to its retrospective character, our study does not include the follow-up findings of the patients.

In conclusion, there is a highly strong relationship between thoracic aortic atherosclerosis and CAD. However, the relationship between EAT volume and CAD is not significant. The presence of aortic atherosclerosis can be used as an additional marker together with traditional cardiovascular risk factors for predicting CAD. In cases when CAC score cannot be evaluated, the presence of aortic atherosclerosis should be a stimulus for investigating CAD. The presence of aortic atherosclerosis detected in routine thorax CT examinations performed for any reason can be a determining factor in predicting CAD particularly in cases with cardiovascular risk factors. Patients with findings of aortic atherosclerosis should be considered as high-risk cases and subjected to a further cardiovascular examination and should be evaluated considering a change in lifestyle and if necessary, considering medical treatment.

## References

- [1] The French Study of Aortic Plaques in Stroke Group. Atherosclerotic disease of the aortic arch as a risk factor for recurrent ischemic stroke. *N Engl J Med* 1996;334:1216–21.
- [2] Fazio GP, Redberg RF, Winslow T, Schiller NB. Transesophageal echocardiographically detected atherosclerotic aortic plaque is a marker for coronary artery disease. *J Am Coll Cardiol* 1993;21:144–50.
- [3] Yorgun H, Hazirolan T, Kaya EB, Canpolat U, Sunman H, Ertuğrul O, Ateş AH, Aksoy H, Aytemir K, Tokgözoğlu L, Kabakçı G, Oto A. Aortic atherosclerosis predicts the extent and severity of coronary atherosclerosis detected by multidetector computed tomography coronary angiography. *Angiology* 2010;61:627–32.
- [4] Chambless LE, Heiss G, Folsom AR, Rosamond W, Szklo M, Sharrett AR, Clegg LX. Association of coronary heart disease incidence with carotid arterial wall thickness and major risk factors: the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1993. *Am J Epidemiol* 1997;146:483–94.
- [5] Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. *Circulation* 1997;96:1432–7.
- [6] Khoury Z, Gottlieb S, Stern S, Keren A. Frequency and distribution of atherosclerotic plaques in the thoracic aorta as determined by transesophageal echocardiography in patients with coronary artery disease. *Am J Cardiol* 1997;79:233–7.
- [7] Taniguchi H, Momiyama Y, Fayad ZA, Ohmori R, Ashida K, Kihara T, Hara A, Arakawa K, Kameyama A, Noya K, Nagata M, Nakamura H, Ohsuzu F. In vivo magnetic resonance evaluation of associations between aortic atherosclerosis and both risk factors and coronary artery disease in patients referred for coronary angiography. *Am Heart J* 2004;148:137–43.
- [8] Takasu J, Mao S, Budoff MJ. Aortic atherosclerosis detected with electron-beam CT as a predictor of obstructive coronary artery disease. *Acad Radiol* 2003;10:631–7.
- [9] Sarin S, Wenger C, Marwaha A, Qureshi A, Go BD, Woomert CA, Clark K, Nassef LA, Shirani J. Clinical significance of epicardial fat measured using cardiac multislice computed tomography. *Am J Cardiol* 2008;102:767–71.
- [10] Nelson MR, Mookadam F, Thota V, Emani U, Al Harthi M, Lester SJ, Cha S, Stepanek J, Hurst RT. Epicardial fat: an additional measurement for subclinical atherosclerosis and cardiovascular risk stratification? *J Am Soc Echocardiogr* 2011;24:339–45.
- [11] Chaowalit N, Somers VK, Pellikka PA, Rihal CS, Lopez-Jimenez F. Subepicardial adipose tissue and the presence and severity of coronary artery disease. *Atherosclerosis* 2006;186:354–9.
- [12] Lee HY, Song IS, Yoo SM, Rho JY, Moon JY, White CS. Can the extent of epicardial adipose tissue thickness or the presence of descending thoracic aortic calcification predict significant coronary artery stenosis in patients with a zero coronary calcium score on multi-detector CT. *Atherosclerosis* 2010;212:495–500.
- [13] Jeltsch M, Klass O, Klein S, Feuerlein S, Aschoff AJ, Brambs HJ, Hoffmann MH. Aortic wall thickness assessed by multidetector computed tomography as a predictor of coronary atherosclerosis. *Int J Cardiovasc Imaging* 2009;25:209–17.
- [14] Kim EJ, Yong HS, Seo HS, Lim SY, Kim SW, Kim MN, Kim YK, Poddar KL, Ramasamy S, Na JO, Choi CU, Lim HE, Kim JW, Kim SH, Lee EM, et al. Association between aortic calcification and stable obstructive coronary artery disease. *Int J Cardiol* 2011;153:192–5.
- [15] Takasu J, Budoff MJ, O'Brien KD, Shavelle DM, Probstfield JL, Carr JJ, Katz R. Relationship between coronary artery and descending thoracic aortic calcification as detected by computed tomography: the Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis* 2009;204:440–6.
- [16] Jang S, Yong HS, Doo KW, Kang EY, Woo OH, Choi EJ. Relation of aortic calcification, wall thickness, and distensibility with severity of coronary artery disease: evaluation with coronary CT angiography. *Acta Radiol* 2012;53:839–44.
- [17] Nallamothu BK, Saint S, Bielak LF, Sonnad SS, Peyser PA, Rubenfire M, Fendrick AM. Electron-beam computed tomography in the diagnosis of coronary artery disease: a meta-analysis. *Arch Intern Med* 2001;161:833–8.
- [18] Tobler HG, Edwards JE. Frequency and location of atherosclerotic plaques in the ascending aorta. *J Thorac Cardiovasc Surg* 1988;96:304–6.
- [19] Tribouilloy C, Peltier M, Andrejak M, Rey JL, Lesbre JP. Correlation of thoracic aortic atherosclerotic plaque detected by multiplane transesophageal echocardiography and cardiovascular risk factors. *Am J Cardiol* 1998;82:1552–5.
- [20] Takasu J, Takanashi K, Naito S, Onishi M, Miyazaki A, Aoyagi Y, Morooka N, Masuda Y, Inagaki Y. Evaluation of morphological changes of the atherosclerotic aorta by enhanced computed tomography. *Atherosclerosis* 1992;97:107–21.
- [21] Wu MH, Chern MS, Chen LC, Lin YP, Sheu MH, Liu JC, Chang CY. Electron beam computed tomography evidence of aortic calcification as an independent determinant of coronary artery calcification. *J Chin Med Assoc* 2006;69:409–14.
- [22] Gondrie MJ, Mali WP, Jacobs PC, Oen AL, van der Graaf Y, PROVIDI Study Group. Cardiovascular disease: prediction with ancillary aortic findings on chest CT scans in routine practice. *Radiology* 2010;257:549–59.
- [23] Wong ND, Gransar H, Shaw L, Polk D, Moon JH. Thoracic aortic calcium versus coronary artery calcium for the prediction of coronary heart disease and cardiovascular disease events. *JACC Cardiovasc Imaging* 2009;2:319–26.
- [24] Bae JH, Bassenge E, Park KR, Kim KY, Schwemmer M. Significance of the intima-media thickness of the thoracic aorta in patients with coronary atherosclerosis. *Clin Cardiol* 2003;26:574–8.
- [25] Couturier G, Voustaniouk A, Weinberger J, Fuster V. Correlation between coronary artery disease and aortic arch plaque thickness measured by non-invasive B-mode ultrasonography. *Atherosclerosis* 2006;185:159–64.
- [26] Djaber R, Schuijff JD, van Werkhoven JM, Nucifora G, Jukema JW, Bax JJ. Relation of epicardial adipose tissue to coronary atherosclerosis. *Am J Cardiol* 2008;102:1602–7.
- [27] Alexopoulos N, McLean DS, Janik M, Arepalli CD, Stillman AE, Raggi P. Epicardial adipose tissue and coronary artery plaque characteristics. *Atherosclerosis* 2010;210:150–4.
- [28] Yorgun H, Canpolat U, Hazirolan T, Sunman H, Ateş AH, Gürses KM, Ertuğrul O, Kaya EB, Aytemir K, Tokgözoğlu L, Kabakçı G, Oto A. Epicardial adipose tissue thickness predicts descending thoracic aorta atherosclerosis shown by multi-detector computed tomography. *Int J Cardiovasc Imaging* 2012;28:911–9.